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IN BRIEF

GENETICS

Convergent evolution exposes selective advantage in CLL

A longitudinal deep-sequencing study in 12 homogeneously treated patients provides the first evidence of convergent subclonal evolution in chronic lymphocytic leukaemia (CLL) pathogenesis. The dominance of subclones harbouring distinct mutations at the same disease loci—*NOTCH1* and *DDX3X* in one patient, and *SF3B1*, *DDX3X* and del(11q23) in another—changed over the course of disease. These findings highlight certain combinations of genetic aberrations that might confer a selective advantage for CLL-cell growth.

Original article Ojha, J. *et al*. Deep sequencing identifies genetic heterogeneity and recurrent convergent evolution in chronic lymphocytic leukemia. *Blood* doi:10.1182/blood-2014-06-580563

HAEMATOLOGICAL CANCER

Flying too close to the sun: loss of IKAROS accelerates CML

Chronic phase-chronic myeloid leukaemia (CP-CML) can progress via an 'accelerated phase' (AP) to acute leukaemia (blast crisis; BC). A new study found that IKAROS, a tumour suppressor involved in B-cell acute lymphoblastic leukaemia, was usually underexpressed or absent in bone-marrow blasts during the AP or BC, compared with CP-CML cells. Expression of dominant negative IKAROS conferred an accelerated-phase phenotype to $CD34^+$ CP-CML cells *in vitro* and in a mouse xenograft model. Thus, loss of IKAROS is implicated in CP-CML progression and has potential diagnostic application.

Original article Beer, P. A. *et al*. Disruption of IKAROS activity in primitive chronic phase CML cells mimics myeloid disease progression. *Blood* doi:10.1182/blood-2014-06-581173

LUNG CANCER

Genomic distinction of multiple primaries from metastases

In patients with non-small-cell lung cancer, distinguishing lung metastases and independent primary lung cancers is challenging and has important clinical ramifications. Murphy *et al*. have now developed a DNA-sequencing-based diagnostic test that holds promise in this regard. The test identified metastases and multiple primary tumours based on the presence or absence, respectively, of shared chromosomal rearrangements, with the genomic data showing good concordance with histological findings. Importantly, no somatic chromosomal breakpoints were shared between any independent primary tumours.

Original article Murphy, S. J. *et al*. Identification of independent primary tumors and intrapulmonary metastases using DNA rearrangements in non-small-cell lung cancer. *J. Clin. Oncol*. doi:10.1200/JCO.2014.56.7644

UROLOGICAL CANCER

PCA3 scoring could improve prostate cancer risk estimation

Prostate cancer antigen 3 (PCA3) scoring, based on urinary PCA3:PSA mRNA ratios, might improve estimation of prostate cancer risk, thereby reducing the need for prostate biopsies. In a validation trial, a PCA3 score >60 had a positive predictive value of 80% and a PCA3 score <20 had a negative predictive value of 88% in men undergoing initial and repeat biopsies, respectively; addition of PCA3 score to the PCPT risk calculator significantly improved the classification of any prostate cancer ($P<0.001$ in both groups), as well as high-grade cancers in men undergoing repeat biopsy ($P\leq0.003$).

Original article Wei, J. T. *et al*. Can urinary PCA3 supplement PSA in the early detection of prostate cancer. *J. Clin. Oncol*. doi:10.1200/JCO.2013.52.8505